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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/039,177 03/13/98 MIYAZONO

K LUD-5539

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HM22/0521

EXAMINER

ROMEO, D

ART UNIT

PAPER NUMBER

1647

21

DATE MAILED:

05/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/039,177

Applicant(s)
Miyazano et al.

Examiner
David Romeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 Jan 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above, claim(s) 1-20, 25, and 27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-24, 26, and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claims 1-28 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☒ Interview Summary (PTO-413) Paper No(s). 21
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☒ Other: *Notice to Comply; Raw Seq List Err Rep*

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DETAILED ACTION

1. In a telephone interview with Mary Anne Schofield on May 14, 2001 a proposed examiner's amendment was discussed that would have potentially placed the application in condition for allowance. Upon further consideration the potential allowability of the claims is
5 withdrawn. New rejections follow.

2. The amendment filed 01/31/2001 (Paper No. 17) has been entered. Claims 1-28 are pending. Claims 1-20, 25, 27 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as drawn to non-elected inventions. Claims 21-24, 26, 28 are being examined to the extent that they read upon methods using agents that promote Smad1 phosphorylation and to
10 the extent that they read upon the elected TGF- β species of agent. Any objection or rejection of record that is not maintained in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The communication filed 03/08/2001 is not fully responsive to the Office communication mailed 07/31/2000 (Paper No. 15) for the reason(s) set forth on the attached Notice To Comply
15 With The Sequence Rules and Raw Sequence Listing Error Report. The above-mentioned reply appears to be *bona fide* attempt to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

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4. Applicants' arguments have been fully considered but they are moot in view of the new grounds of rejection that follow.

New formal matters, objections, and/or rejections:

Specification

5. The disclosure is objected to because of the following informalities: on page 1 after the title and before "Field of the Invention" the priority data indicates that the instant application is a C-I-P of itself.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. Claims 21-24, 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to or encompass a "molecule" or "agent" that binds ALK-1, wherein the binding phosphorylates Smad1, and wherein the phosphorylation of Smad1 enhances expression of a gene. The specification teaches that ALK-1 binds TGF- β 1 and activin A but the functional consequences of this binding remain to be elucidated (sentence bridging pages 33-34); ALK-1 is a receptor for TGF- β (page 35, lines 7-8); a constitutively active form of ALK-1

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phosphorylated Smad1 (paragraph bridging pages 35-36); and, TGF- β binds to ALK-1 leading to phosphorylation of Smad1 (page 37, lines 6-7). Although working examples are not required, the specification provides no examples of the enhancement of gene expression as a result of the interaction of TGF- β and ALK-1 and the phosphorylation of Smad1 thereby, and the functional consequences of this binding remain to be elucidated (specification at sentence bridging pages 33-34). There is nothing in the instant specification or in the prior art of record to suggest that the interaction of TGF- β and ALK-1 and the phosphorylation of Smad1 thereby enhances or inhibits gene expression. The specification lacks guidance for the enhancement of gene expression. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

7. Claims 21, 22, 26, 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a TGF- β that binds ALK-1, does not reasonably provide enablement for a "molecule" or "agent" that binds ALK-1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are directed to or encompass a "molecule" or "agent" that binds ALK-1, wherein the binding phosphorylates Smad1, and wherein the phosphorylation of Smad1 enhances expression of a gene. The

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specification teaches that ALK-1 binds TGF- β 1 and activin A but the functional consequences of this binding remain to be elucidated (sentence bridging pages 33-34); ALK-1 is a receptor for TGF- β (page 35, lines 7-8); a constitutively active form of ALK-1 phosphorylated Smad1 (paragraph bridging pages 35-36); and, TGF- β binds to ALK-1 leading to phosphorylation of Smad1 (page 37, lines 6-7). However, no other molecules or agents are described that bind the extracellular domain, or any other domain, of ALK-1, phosphorylate Smad1, and enhance gene expression. The limitations "molecule" and "agent" are analogous to a single means claim of the type disparaged by the court. A single means claim, i.e., where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. The problem with the limitations "molecule" and "agent" are that they cover every conceivable means which achieves the desired activity, whereas the specification discloses at most a TGF- β or an ALK-1 extracellular domain binding portion thereof.

As such, the terms "molecule" and "agent" encompasses compounds that are structurally unrelated to TGF- β . The specification fails to teach the skilled artisan how to make such structurally unrelated compounds that have the desired activity or will perform in the manner instantly disclosed. Furthermore, the instant specification does not identify those structural features of a "molecule" or "agent" which are essential for the desired activity those which are

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not. In the absence of this information a practitioner would have to resort to a substantial amount of unduly extensive experimentation in the form of random analysis of all "molecules" and "agents" before they could even begin to rationally make a "molecule" or "agent" other than TGF- β . The disclosure of a single species of "molecule" and "agent", i.e. TGF- β , is clearly insufficient support under 35 U.S.C. § 112, first paragraph, for claims which encompass any and all "molecules" or "agents".

8. Claims 21, 22, 26, 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to or encompass a "molecule" or "agent" that binds ALK-1, wherein the binding phosphorylates Smad1, and wherein the phosphorylation of Smad1 enhances expression of a gene. The specification teaches that ALK-1 binds TGF- β 1 and activin A but the functional consequences of this binding remain to be elucidated (sentence bridging pages 33-34); ALK-1 is a receptor for TGF- β (page 35, lines 7-8); a constitutively active form of ALK-1 phosphorylates Smad1 (paragraph bridging pages 35-36); and, TGF- β binds to ALK-1 leading to phosphorylation of Smad1 (page 37, lines 6-7). However, no other molecules or agents are described that bind the extracellular domain, or any other domain, of ALK-1, phosphorylate Smad1, and enhance gene expression. The specification and

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claims do not indicate what distinguishing attributes are shared by a "molecule" or "agent" such that they would function as intended. The specification and claims do not place any limit on the structure of the "molecule" or "agent". Thus, the scope of the claims include numerous structural variants, and the genus is highly variant because an unlimited number of structural differences

5 between members of the "molecule" or "agent" genus is permitted. The specification and claims do not provide any guidance as to what "molecules" or "agents" should be made. No common structural attributes identify the members of the "molecule" or "agent" genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common

10 attributes or characteristics that identify members of the genus, and because the genus is highly variant, TGF- β alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. The claims encompass subject matter not supported by an adequate written description because a representative number

15 of species have not been described.

Conclusion

9. No claims are allowable. Claim 28 may be allowable upon cancellation of the non-elected subject matter and limiting the claim to an "agent" wherein the "agent" is TGF- β .

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ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 6:45 A.M. TO 3:15 P.M.

5 IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

OFFICIAL PAPERS FILED BY FAX SHOULD BE DIRECTED TO (703) 308-4242.

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

10 
DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

MAY 19, 2001

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING
NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: _____

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

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